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EXAMINER	
ANGELL, JON E	

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1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/668,050	BRATZLER ET AL.	
	Examiner	Art Unit	
	J. E. Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,21,31 and 36-71* is/are pending in the application.

4a) Of the above claim(s) *5,6,21,31,36,38-40,42 and 48-71* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,7-17,37,41 and 43-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 1/7/08.

Claims 1-17, 21, 31, 36-71 are currently pending in the application and are addressed herein.

Election/Restrictions

1. Applicant's election with traverse of Group I and the species Taxol and skin cancer in the reply filed on 1/7/08 is acknowledged. The traversal is on the ground(s) that claims 10 and 11 should be rejoined with the claims of Group I. It is noted that Applicants have presented no other arguments with respect to any claims other than claims 10 and 11. After further consideration, Applicants argument with respect to claims 10 and 11 are persuasive and claims 10 and 11 are rejoined with the claims of Group I. However, since no arguments have been set forth with respect to the restriction of any claims other than 10 and 11, the restriction requirement for the claims of Groups II-XI other than claims 10 and 11 are is still deemed proper and is therefore made FINAL.

2. Claims 5, 6, 21, 31, 36, 38-40, 42, 48-71 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/7/08. It is noted that claim 5 (which was indicating as belonging to Groups I, II and III) reads on the method of claim 2 wherein the cancer vaccine is selected from a group of cancer vaccines. However, the elected invention does not encompass the cancer vaccine of claim 2, therefore, claim 5 has been withdrawn from consideration and is consider to properly belong with Group III.

3. Claims 1-4, 7-17, 37, 41, 43-47 are examined herein.

Claim Rejections - 35 USC § 112, first paragraph

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-4, 7-17, 37, 41, 43-47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

> A method for inhibiting tumor cell growth in a subject having cancer, wherein said method comprises administering to said subject:
>
> a) a poly-G nucleic acid; and
>
> b) a cancer medicament;
>
> wherein the poly-G nucleic acid is not conjugated to the cancer medicament, and wherein the administration of said poly-G nucleic acid and said cancer medicament results in the inhibition of tumor cell growth in said subject;

does not reasonably provide enablement for the full scope encompassed by the claims. Specifically, the specification is not enabling for a method of preventing/curing cancer in a subject. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988).

Wands states on page 1404,
"Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The nature of the invention

The instant claims are drawn to methods of treating and preventing or curing of cancer using a poly-G nucleic acid in combination with a cancer medicament.

The breadth of the claims

The claims are very broad. The broadest claims (e.g. claim 1) encompass treating or preventing any type of cancer by administering to a subject any poly-G nucleic acid and any cancer medicament.

The unpredictability of the art and the state of the prior art

As mentioned above, the specification does not enable the claims for prevention or curing of cancer. At the time of filing there were no methods known in the art for using immunostimulatory oligonucleotides in combination with a cancer medicament for the prevention/curing of cancer.

The relevant art teaches that immunotherapy of cancer with regards to preventing/curing cancer is unpredictable. For instance, **Gouttefangeas et al.** (Nature Biotechnology Vol. 18:491-

492; 2000) teaches, "effective immunotherapy has remained elusive because of three major problems: first, for many tumors, no or not enough suitable antigens are known; second, no consensus exists for the best antigen formulations or the rout of immunization; and third, tumors under immune attack tend to be selected for antigen loss variants." (See p. 491, first paragraph). Specifically regarding the immunostimulatory effects of oligodeoxynucleotides, Gouttefangeas points out, "[W]e do not yet know whether such constructs [immunostimulatory oligonucleotides] work in humans. Some immunostimulatory effects of CpG motifs have been described in human peripheral blood in vitro, most notably in dendritic cells, but immunization trials have not been reported. Thus, the efficacy of CpG-protein constructs for immunotherapy in patients remains to be tested." (See p. 492, middle column, first paragraph). Therefore, Gouttefangeas teaches that there has been no identification of any cancer immunizing oligonucleotides in humans. Thus no "master drug" has been identified for curing or preventing cancer.

Furthermore, **Old** (Scientific American 1996), teaches that there are several problems associated with cancer immunotherapy. For instance, Old teaches, "Despite the great hope of immunotherapy, a dark cloud hangs over all our attempts to control cancer by immune mechanisms. Cancer cells are masters of deceit and disguise-veritable Houdinis that can readily alter themselves to evade immunological recognition and attack." (See p. 11, under "The hurdles ahead"). Furthermore, Old teaches, "[I]t is conceivable that cancer vaccines may injure normal cells to some degree" and points out, "There are a number of disease states, called autoimmune diseases, that arise when the immune system turns against normal tissues in the body." (See p. 11, under "The hurdles ahead"). Finally, Old teaches, "[W]e need to exert considerable caution

in making any predictions" clearly indicating the unpredictable nature of immunotherapy (See p. 11, under "The hurdles ahead").

Although the methods reviewed by Old encompass immunotherapy in general (and very broadly) the problems indicated by Old are relevant to the presently claimed invention because the basic mechanism—immune response directed to cancer cells displaying cancer-specific antigens—are the same, even if the claimed method steps are not identical.

Furthermore, it is respectfully pointed out that the claims encompass preventing/curing cancer in a subject. Preventing cancer using the instant method encompasses administering the therapeutic compounds to individuals who do not have cancer, and would encompass administering the immunostimulatory nucleic acid and the cancer medicament (such as a chemotherapeutic drug) to normal (i.e. cancer-free) individuals. Considering the teachings of the prior art and considering that the instant invention encompasses administering an immunostimulatory agent and agent intended to lyse cells (i.e. the cancer medicament), it is clear that there are a number of obstacles that must be overcome before the claimed invention could be used to prevent cancer in a subject.

Additionally, there is no indication in the prior art or in the post filing art that there is any method which can be used to cure or prevent the future occurrence of cancer in a subject.

In fact, **Bodey et al.** (Anticancer Research Vol. 20:2665-2676; 2000) teaches,

> "Although general immune activation directed against the target antigens contained within the cancer vaccine has been documented in most cases, reduction in tumor load has not been frequently observed, and tumor progression and metastasis usually ensue, possibly following a slightly extended period of remission. The failure of cancer vaccine to fulfill their promise is due to the very relationship between host and tumor: through a natural selection process the host leads to the selective enrichment of clones and highly aggressive neoplastic transformed cells…", "The use of cancer vaccines seems, at present, destined to remain limited to their employment as adjuvants to both traditional

> therapies and in the management of minimal residual disease following surgical resection or the primary cancer mass." (See p. 2665, abstract, second column); and,
>
> "[T]he cancer vaccine approach to immunotherapy has been shown in most cases to result in an in vitro or s.c.... enhancement of TAA targeted immunity. However, even after considerable remission (which has not been shown to be strictly induced by vaccination), the malignant tumor does in most cases progress and overwhelm the host. This apparent contradiction is the defining characteristic of the difficulties associated with an immunological approach to cancer therapy, including the generation of cancer vaccines." (See p. 2673, first column).

Therefore, Bodey clearly indicates that recurrence of cancer after initial successful treatment of a tumor with an immunotherapeutic composition is common, indicating unpredictability in curing or preventing the future occurrence of cancer in a subject.

Working Examples and Guidance in the Specification

The specification has no working examples, whatsoever, of effective treatment of any type of cancer using the claimed composition. The specification does disclose a variety of precise protocols for the administration of the composition. However, no data is presented supporting the notion that the claimed invention is an effective cancer treatment. Nor does the specification disclose any working examples or guidance which overcome the unpredictability of cancer therapy, as recognized in the art. Furthermore, no guidance is provided as to the dosage amount or frequency required to effectively treat cancer. It would essentially be a trial and error process to make and use the diverse species of therapeutic molecules encompassed by the claims. Therefore, without any supporting data, it is not predictable that the claimed treatment method would effectively achieve any therapeutic benefit.

It is acknowledged that the specification discloses guidance on the administration of the therapeutic compounds to a subject, thus indicating how to administer the compounds, but there is no disclosure indicating that the method could prevent the occurrence of any future cancer.

Quantity of Experimentation

As mentioned above, there are a number of problems related to immunotherapy which apply to the claimed method, including autoimmune disorders, as well as the ability of cancer cells to adapt and evade the immune response. Furthermore, the claims encompass the prevention of cancer and the relevant art does not teach any methods which can be used to prevent cancer in a subject. Therefore, in order to practice the claimed invention to prevent cancer in a subject one of skill in the art would have to perform additional experimentation. The additional experimentation would require the testing of the method in cancer-free individuals to test for the possibility that the method could result in autoimmune disease. Furthermore, the experimentation would have to indicate that the method could be used to prevent any future occurrence of any type of cancer in the subject. This would require years of experimentation in order to show that the treatment could prevent any future occurrence of cancer.

Level of the skill in the art

The level of the skill in the art is deemed to be high.

Conclusion

Considering the of unpredictable nature of cancer prevention, the breadth of the claims, the lack of any working examples in the specification; and the high degree of skill required, it is concluded that the amount of experimentation required to perform the broadly claimed method to its full scope (i.e., preventing cancer) is undue.

Claim Rejections - 35 USC § 112, second paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 10 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. Claim 10 recites the limitation "the immunostimulatory nucleic acid" in line 1. There is insufficient antecedent basis for this limitation in the claim. It will be assumed that "the immunostimulatory nucleic acid" of claim 10 is referring to the "poly-G nucleic acid" of claim 1. Claim 11 depends on claim 10 and is therefore also rejected for the same reason.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1, 2, 10-14, 37 are rejected under 35 U.S.C. 102(e) as being anticipated by Bennett et al. (US Patent 6,172,216 B1).

The instant claims are drawn to (in general) a method for treating cancer in a subject by administering a poly-G nucleic acid and a cancer medicament.

Bennett clearly teaches a method of treating cancer in a subject by administering to the subject an oligonucleotide sequence that is a 20mer wherein the oligonucleotide comprises the sequence CTGGGCC (see SEQ ID NO: 10, Table 1, column 27). It is pointed out that the specification indicates that the immunostimulatory poly-G nucleic acid preferably comprises the sequence XXGGGXX (see p. 12, lines 20-30 of the specification). Therefore, the oligonucleotide meets all of the structural limitations set forth in the specification to be an immunostimulatory poly-G nucleic acid. Furthermore, Bennett also teaches that the oligonucleotide can be combined with a cancer chemotherapeutic compound (which would not be conjugated to the oligonucleotide) to form a pharmaceutical composition (e.g., see claims 1, 11 and 34). Bennett indicates that the oligonucleotide/chemotherapeutic composition can be used to treat cancer (e.g., see Col. 1, lines 1-10; Col. 1, line 65 through Col. 2, line 21; and Col. 15, lines 12-65). Bennett also teaches that the oligonucleotide can comprise a modified backbone, including a phosphorothioate-modified backbone (e.g., see Col. 6, line 55 through Col. 7, line 10). It is also pointed out that the Bennett's oligonucleotide that is SEQ ID NO: 10, is free of any CpG motifs and poly-T motifs. Furthermore, Bennett also teaches that the oligonucleotides can be comprised in a liposome (see column 10, lines 50-64), which would constitute a "colloidal dispersion system" as indicated in instant claim 37 (e.g., see instant claim 39).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1, 3, 7-9, 12, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett (US 6,172,216) in view of Muller (WO 97/32604).

Claims 1 and 12 are rejected by Bennett's teaching of a method for treating cancer in a subject by administering to the subject a 20mer oligonucleotide sequence comprising the sequence CTGGGCC (see SEQ ID NO: 10, Table 1, column 27). It is pointed out that the specification indicates that the immunostimulatory poly-G nucleic acid preferably comprises the sequence XXGGGXX (see p. 12, lines 20-30 of the specification). Therefore, the oligonucleotide meets all of the structural limitations set forth in the specification to be an immunostimulatory poly-G nucleic acid. Furthermore, Bennett also teaches that the oligonucleotide can be combined with a cancer chemotherapeutic compound (not conjugated) to form a pharmaceutical composition (e.g., see claims 1, 11 and 34). Bennett indicates that the oligonucleotide/chemotherapeutic composition can be used to treat cancer (e.g., see Col. 1, lines 1-10; Col. 1, line 65 through Col. 2, line 21; and Col. 15, lines 12-65). Bennett also teaches that

the oligonucleotide can comprise a modified backbone, including a phosphorothioate-modified backbone (e.g., see Col. 6, line 55 through Col. 7, line 10). It is also pointed out that the Bennett's oligonucleotide that is SEQ ID NO: 10, is free of any CpG motifs and poly-T motifs.

Bennett does not teach that 1) the chemotherapeutic agent is Taxol/Paclitaxel (claims 3, 7, 15); 2) the cancer medicament is a hormone therapy (claim 6); 3) the method further comprises administering IFN-alpha to the subject (claims 8, 16); and 4) the cancer is skin cancer (claim 9).

However, Muller teaches a method of treating cancer using a combination therapy comprising administering to a subject a composition comprising an oligonucleotide sequence (not a poly-G oligonucleotide) in combination with a chemotherapeutic agent, such as taxol, a hormonal agent, and interferon-alpha (IFN-alpha) (e.g., see p. 1, first full paragraph; p. 32, lines 10-15; p. 33, under p(E); and p. 34, under (F) and (I)). Furthermore, Muller indicates that the combination therapy could be used to treat a variety of cancers, such as melanoma (a form of skin cancer) (e.g., see p. 26, lines 1-5).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to make the claimed invention using the teachings of Bennett and Muller with a reasonable expectation of success. In order to make the claimed invention one of skill in the art could combine the references such that the method of Bennett is modified so that the therapeutic composition that is administered to the subject comprises the poly-G nucleic acid taught by Bennett in combination with taxol, a hormonal agent, and further comprises IFN-alpha for the treatment of a skin cancer, as taught by Muller.

11. Claims 1, 2 and 4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett (US 6,172,216) in view of Dannenberg (US Patent 6,403,630).

Claims 1 and 2 are rejected by Bennett's teaching of a method for treating cancer in a subject by administering to the subject an oligonucleotide sequence comprising the sequence CTGGGCC (see SEQ ID NO: 10, Table 1, column 27). It is pointed out that the specification indicates that the immunostimulatory poly-G nucleic acid preferably comprises the sequence XXGGGXX (see p. 12, lines 20-30 of the specification). Therefore, the oligonucleotide meets all of the structural limitations set forth in the specification to be an immunostimulatory poly-G nucleic acid. Furthermore, Bennett also teaches that the oligonucleotide can be combined with a cancer therapeutic compound (not conjugated) to form a pharmaceutical composition (e.g., see claims 1, 11 and 34). Bennett indicates that the oligonucleotide/cancer therapeutic composition can be used to treat cancer (e.g., see Col. 1, lines 1-10; Col. 1, line 65 through Col. 2, line 21; and Col. 15, lines 12-65). Bennett also teaches that the oligonucleotide can comprise a modified backbone, including a phosphorothioate-modified backbone (e.g., see Col. 6, line 55 through Col. 7, line 10). It is also pointed out that the Bennett's oligonucleotide that is SEQ ID NO: 10, is free of any CpG motifs and poly-T motifs.

Bennett does not teach that the cancer therapeutic agent is Herceptin (claim 4).

However, Dannenberg teaches a method for treating cancer comprising administering to a subject having cancer a composition comprising the combination of two anti-cancer agents, one of which is Herceptin (e.g., see abstract; Col. 1, lines 19-36; Col. 2, lines 4-15; Col. 11, lines 15-45; and claim 1).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to make the claimed invention using the teachings of Bennett and Dannenberg with a reasonable expectation of success. In order to make the claimed invention one of skill in the art could combine the references such that the method of Bennett is modified so that the therapeutic composition that is administered to the subject comprises the poly-G nucleic acid taught by Bennett in combination with Herceptin as taught by Dannenberg.

12. Claims 1, 2, 12 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett (US 6,172,216) in view of Eberlein (US Patent 5,550,214).

Claims 1, 2 and 12 are rejected by Bennett's teaching of a method for treating cancer in a subject by administering to the subject an oligonucleotide sequence comprising the sequence CTGGGCC (see SEQ ID NO: 10, Table 1, column 27). It is pointed out that the specification indicates that the immunostimulatory poly-G nucleic acid preferably comprises the sequence XXGGGXX (see p. 12, lines 20-30 of the specification). Therefore, the oligonucleotide meets all of the structural limitations set forth in the specification to be an immunostimulatory poly-G nucleic acid. Furthermore, Bennett also teaches that the oligonucleotide can be combined with a cancer therapeutic compound (not conjugated) to form a pharmaceutical composition (e.g., see claims 1, 11 and 34). Bennett indicates that the oligonucleotide/cancer therapeutic composition can be used to treat cancer (e.g., see Col. 1, lines 1-10; Col. 1, line 65 through Col. 2, line 21; and Col. 15, lines 12-65). Bennett also teaches that the oligonucleotide can comprise a modified backbone, including a phosphorothioate-modified backbone (e.g., see Col. 6, line 55 through

Col. 7, line 10). It is also pointed out that the Bennett's oligonucleotide that is SEQ ID NO: 10, is free of any CpG motifs and poly-T motifs.

Bennett does not teach that the cancer therapeutic agent is a cancer antigen, such as a Her2/neu peptide (claim 17).

However, Eberlein teaches a method for treating cancer comprising administering to a subject having cancer a composition comprising the cancer antigen that is a Her2/neu peptide (e.g., see abstract, Col. 2, lines 25-50; Col. 17, lines 58-67).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to make the claimed invention using the teachings of Bennett and Eberlein with a reasonable expectation of success. In order to make the claimed invention one of skill in the art could combine the references such that the method of Bennett is modified so that the therapeutic composition that is administered to the subject comprises the poly-G nucleic acid taught by Bennett in combination with the cancer antigen Her2/Neu peptide taught by Eberlein.

13. Claims 41-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bennett (US 6,172,216) in view of Muller (WO 97/32604), Kasid et al. (WO 98/43095), and Mathiowitz et al. (WO 95/24929).

Claims 1 and 12 are rejected by Bennett's teaching of a method for treating cancer in a subject by administering to the subject a 20mer oligonucleotide sequence comprising the sequence CTGGGCC (see SEQ ID NO: 10, Table 1, column 27). Furthermore, Bennett also teaches that the oligonucleotide can be combined with a cancer chemotherapeutic compound (not conjugated) to form a pharmaceutical composition (e.g., see claims 1, 11 and 34). Bennett

indicates that the oligonucleotide/chemotherapeutic composition can be used to treat cancer (e.g., see Col. 1, lines 1-10; Col. 1, line 65 through Col. 2, line 21; and Col. 15, lines 12-65). Bennett also teaches that the nucleic acid can be synthetic (e.g. see column 9, lines 47-56).

Bennett does not teach that 1) the oligonucleotide is administered in an implant (claim 41); 2) the cancer is skin cancer (claim 45); 3) the nucleic acid is administered following radiation (claim 46).

Mathiowitz teaches a polymeric gene delivery system that comprises an implant for delivering a therapeutic nucleic acid to a subject (e.g. see abstract; page 9, line 15 through page 7; etc.). It is also noted that the instant specification discloses that the implant system of Mathiowitz is specifically encompassed by the instant invention (e.g., see page 54).

Muller teaches a method of treating cancer using a combination therapy comprising administering to a subject a composition comprising an oligonucleotide sequence (not a poly-G oligonucleotide) in combination with a chemotherapeutic agent, (e.g., see p. 1, first full paragraph; p. 32, lines 10-15; p. 33, under p(E); and p. 34, under (F) and (I)). Furthermore, Muller indicates that the combination therapy could be used to treat a variety of cancers, such as melanoma (a form of skin cancer) (e.g., see p. 26, lines 1-5).

Additionally, radiation was a well known therapy for treating cancer. For example, Kasid teaches that an antisense oligonucleotide that is has anti-cancer function increases the efficacy of radiation treatment (e.g., see abstract; pages 1-2; etc.)

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time of filing to make the claimed invention using the teachings of Bennett, Mathiowitz , Kasid and Muller with a reasonable expectation of success. In order to make the claimed invention one

of skill in the art could combine the references such that the method of Bennett is modified so that the therapeutic composition that is administered to the subject comprises the poly-G nucleic acid taught by Bennett in the implant taught by Mathiowitz, for the treatment of a skin cancer as taught by Muller, and wherein the oligonucleotide is administered in order to increase the efficacy of radiation treatment as taught by Kasid.

MPEP 2144.06, in discussing art-recognized equivalence for the same purpose, mentions *In re Kerkhoven*, wherein the court expressed the following:

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose…[T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven* 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

In the instant case, the antisense oligonucleotides of Bennett and the radiation treatment of Kasid are considered to be two compositions each of which is taught by the prior art to be useful for the same purpose (treating cancer).

Furthermore, it would have been a matter of routine experimentation to test different administration protocols of administering the therapeutics, including administering the oligonucleotide after radiation treatment in order to determine the effective as well as the optimal order of administrations (see in *In re Aller*, 105 USPQ 233 at 235). Routine optimization is not considered inventive and no evidence has been presented that the selection of administering the oligonucleotide after radiation treatment was other than routine, that the result from the

optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/
Primary Examiner, Art Unit 1635